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(54) Title: HYDROGELS CONTAINING CROSS-LINKED CARBOXYLIC ACID-HYDROXY ALCOHOLPOLYMERS FOR USE IN DRUG DELIVERY

(57) Abstract

Provided is a material comprised of hydrogels containing cross-linked carboxylic acid-hydroxy alcohol polymers. The present invention results in a material which absorbs up to 20 times or greater of its weight in water, and simultaneously administer an effective amount of a drug to an action site. The end-use characteristics have also been found to be quite stable, non-sticky, free of smell yet pliable and conforming. As a result, it is also applicable for use as a bandage, article, pad, dressing, patch or alike.

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HYDROGELS CONTAINING CROSSLINKED CARBOXYLIC ACID-HYDROXY ALCOHOL POLYMERS FOR USE IN DRUG DELIVERY

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. application, entitled "Hydrogels Containing Crosslinked Carboxylic Acid-Hydroxy Alcohol Polymers For Use In Drug Delivery", filed February 5, 1998.

FIELD OF THE INVENTION

The present invention relates to a material comprised of hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers of drug delivery. The present invention also relates to articles employing such material. In particular, such articles can be employed in bandages, wiping cloths, dressings, pads, patches and alike.

BACKGROUND OF THE INVENTION

Beneficial therapeutic effects would result from the use of a bandage, dressing or alike for wounds that would not irritate the wound while providing comfort to the wound. Accordingly, it is an object of the present invention to provide a material which would be useful for treating a wound, and which would provide comfort in dressing the wound.

Beneficial therapeutic effects would also result from the use of a bandage, dressing or alike that would deliver an effective and sustained release amount of an antibiotic, antimicrobial, antibacterial or other drug to the wound. Consequently, yet another object of the present invention is to provide a material that would be in a form of a dressing, bandage or alike, that would be applied to the wound and that would also deliver a sustained release amount of the drug to the wound.

Beneficial therapeutic effects and improved patient compliance would result from the utilization of a material that would protect a desired drug from adverse biological environments and guarantee a sustained release of the drug over time. Consequently, an additional object of the present invention is to provide a material that would protect the drug and that would guarantee a sustained release of the drug, and thus, the material would allow for the use of lower dosages and less

frequent administration of the drug.

Yet another object of the present invention is to provide articles employing the foregoing material.

These and other objects of the present invention will become apparent upon a review of the following specification and the claims appended thereto.

SUMMARY OF THE INVENTION

In accordance with the foregoing objectives, there is provided a material comprised of hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers. The hydrogels of the present invention are prepared by reacting crosslinked polycarboxylic acid polymers with a polyhydroxy alcohol monomers and/or oligomers. The crosslinked polycarboxylic acid polymer may include crosslinked polyacrylic acid or a crosslinked methacrylic acid polymer. In another embodiment, the polyhydroxy alcohol monomer may be a glycerine. The reaction of polyhydroxy alcohol monomers and/or oligomers with crosslinked polycarboxylic acid polymers of the present invention produces a hydrogel that is capable of absorbing up to about 20 times its weight in water and can simultaneously deliver an effective amount of a desired drug. The material of the present invention is stable, can be made sticky or non-sticky depending on the application, free of smell yet pliable and conforming. As a result, the present invention may also be used in bandages, dressings or other pads for the treatment of a wound or for delivery of a drug to the site of action.

DETAILED DESCRIPTION OF THE INVENTION

Hydrogels are crosslinked three-dimensional hydrophilic polymer networks that swell, but do not dissolve, when brought in contact with water. The material of the present invention comprises hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers. The hydrogels of the present invention are prepared by reacting crosslinked polycarboxylic acid polymers with polyhydroxy alcohol monomers and/or oligomers.

The crosslinked polycarboxylic acid polymer of the present invention includes crosslinked polyacrylic acid (and its derivative) or crosslinked methacrylic acid polymer. Examples of commercially available crosslinked polyacrylic acid polymers include tradename 1460 from Chemdal Chemical Co. and tradenames CARBOPHIL and CARBOPOLE from B.F. Goodrich Co. Other crosslinked polycarboxylic acid polymers that may be used in the present invention include crosslinked polymaletic acid anhydride and crosslinked polytrimaletic acid anhydride. It is preferred that the acid is essentially in the free acid form.

The polyhydroxy alcohol monomer and/or oligomer of the present invention includes monoglycerine, glycol, pentaerythritol, pentose, hexose, diglycerine, triglycerine, diethylene glycol, triethylene glycol, decaglycol, decapropylene glycol, or any other polyhydroxy alcohol monomer or oligomer that can be liquified without degradation of the monomer or oligomer. It was found that the lower the viscosity of the liquid polyhydroxy alcohol monomer or oligomer, the faster the plasticizing action occurred.

When added to and blended with the crosslinked polycarboxylic acid polymer, the polyhydroxy alcohol monomer and/or oligomer of the present invention plasticizes the polymer, reacts with the carboxylic group to form an ester, and thus, creates a thermoset material. A decrease in the particle size of the crosslinked polycarboxylic acid polymer powder results in a faster diffusion and plasticizing of the powder with the polyhydroxy alcohol monomer or oligomer. In addition, a decrease in the particle size of the crosslinked polycarboxylic acid polymer powder should result in a smoother surface of the hydrogel.

During the reaction, the thermoset material may be casted in any desired end-product form including a film or thread. For example, such a material may be produced so as to be soft or non-sticky or free of odor yet pliable and conforming. In another example, the material may also be produced in a form and texture to simulate human skin.

The crosslinked polycarboxylic acid polymer and polyhydroxy alcohol monomer or oligomer may be mixed, blended and reacted using any conventional method. In one example, the polyhydroxy alcohol monomer or

oligomer and the crosslinked polyacrylic acid polymer (or other crosslinked polymer of carboxylic acid) may be compounded to form a mixture. In one embodiment, the weight ratio of glycerine to polycarboxylic acid polymer can range widely, for example, from 1:9 to 9:1. In another embodiment, the weight ratio ranges from 6:4 to 2:8, and, in another embodiment, from 4:6 to 2:8 and another 3:7. In another example, the mixture can then be extruded to form a suitable film, thread or other shaped article. Other methods of forming the desired article include employing a press to form sheets and a cutter to form pads or strips. In another embodiment, the shaped article may be laminated to a suitable backing such as a fabric or substrate.

One of the many advantages which the hydrogels of the present invention have is the less complex method required to produce the hydrogels. Specifically, in one example, the process only involves mixing and reacting a commercially available crosslinked polyacrylic acid polymer powder with a commercially available polyhydroxy alcohol monomer or oligomer. As a result, the final end-use characteristics of the material may be more closely controlled. For example, the molarity of the carboxylic acid group of the crosslinked polycarboxylic acid polymer may be adjusted and thus, the carboxylic acid groups that are available to react may also be controlled. Another advantage of the present invention is the hydrogel, which is produced from the process of the present invention, has a high amount of carboxylic acid groups available and thus, a high amount of reaction sites available for charging with a desired drug.

Because of the presence of the polyhydroxy alcohol monomer or oligomer, heating the material will cause some crosslinking with the polycarboxylic acid polymers by creating an ester between the alcohol group and the acid group. Thus, the material becomes thermoset. As such, the amount of water absorbed by the material can be precisely controlled by the amount of crosslinking of the material. The more material is crosslinked, the less carboxylic acid groups available in the hydrogel and thus, the less water the material can absorb. Therefore, when it is desired to have a material with a high water absorption, the amount of crosslinking should be minimized and thus, a high percentage of

carboxylic acid groups remain available in the hydrogel. Consequently, the amount of crosslinking of the material may be controlled by adjusting the process parameters including: (a) the amount of polyhydroxy alcohol monomer or oligomer added to the blend; (b) the temperature of any extrusion or treatment; and (c) the time the material is exposed to the heat treatment.

One method of determining the amount of carboxylic acid group available in the hydrogel and thus, the amount of carboxylic acid groups available for charging with a desired drug, is employing a back titration method. One example of this method includes the following steps: (1) drying the hydrogel to remove any residual moisture; (2) immersing the hydrogel in a 0.1N sodium hydroxide solution for about 1 hour; (3) removing the hydrogel from the solution after the hydrogel reaches equilibrium with the solution (i.e. no further swelling); (4) washing the excess liquid from the hydrogel and adding this solution back to the hydroxide solution; (5) titrating the sodium hydroxide solution (e.g. using sulfuric acid and a methyl red indicator/pH indicator/pH meter) to determine the amount of sodium hydroxide that reacted with the hydrogel.

In addition, characteristics of the end product of the present invention can be modified or changed by controlling the process variables including: (a) the acid/polyhydroxy alcohol ratio; (b) the temperature during crosslinking; and (c) the time during crosslinking. Consequently, by adjusting the above variables, a material according to the present invention may be produced to have the desired end-use characteristics including soft or non-sticky or pliable or tacky or brittle.

Accordingly, the material of the present invention, which is comprised of hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers, may be used as an absorbent material to absorb aqueous solutions. As well, the material in a swollen state, where it has already been immersed in an aqueous solution, can be used as a suitable dressing or bandage to help comfort and heal a wound.

Other applications for the present invention include charging the material of the present invention with a desired drug and then applying the material

to a specific site of action. As a result, the desired drug would: (a) deliver a sustained amount and controlled release of the drug over time to the action site; and (b) protect the drug from adverse biological environments. Consequently, the material of the present invention may allow for the use of lower dosages and less frequent administration of the drug and thus, may result in beneficial therapeutic effects and improved patient compliance. Examples of such action sites include ocular delivery, nasal delivery, transdermal delivery, buccal delivery, rectal delivery and other delivery routes.

The material of the present invention may also be charged with an antibiotic, hormone, enzyme, anesthetic or other beneficial pharmacological drugs that solubilize in the aqueous solution, which is absorbed by the material, and that are then applied to the action site. Thus, the material would have the characteristic of sustained release of the drug over time to the action site. This controlled release characteristic also permits one to place the material of the present invention, which is charged with the desired drug, on a large area of the body without fear of overexposing the body to the drug. In another application, the material may be produced so that the material can be used as an ion exchange membrane.

In one embodiment, the polyhydroxy alcohol monomer or oligomer is chosen so that the ratio of hydroxy groups to carbon is in the range of about 1:1 to about 1:10. In further embodiments, the ratio of hydroxy groups to carbon for the polyhydroxy alcohol monomer or oligomer may include 2:3 (e.g. hexose), 1:3 (e.g. dipropylene glycol) and 1:10 (e.g. decaethylene glycol). For example, glycerine has a ratio of 1:1 of hydroxy groups to carbon. The advantage of employing a polyhydroxy alcohol monomer or oligomer with a ratio of about 1:1 (ratio of hydroxy groups to carbon) is that the monomer or oligomer is more hydrophilic and thus, (a) diffuses more readily with the polycarboxylic acid polymer, (b) displays a faster plasticizing action, and (c) when plasticising action occurs, the material coalesces that allows one polyalcohol molecule to react with two carboxylic acid particulates, and results in a chemical fusion. In another embodiment, the polyhydroxy alcohol monomer or oligomer may have an average molecular weight in the range of about 62 to about 500.

For example, the non-sticky, odor free, yet pliable and conforming nature of the material in a partial swollen state (by being partially charged with water or aqueous solution) is suitable for use as a bandage, dressing, pad or alike for a wound or treatment of a particular infection or disease. When applied to a wound such as a burn, the non-stickiness of a film or other desired shape comprised of the material in the present invention provides comfort. Since, in one embodiment, the material is only in a partially swollen state (i.e. has not absorbed the maximum amount of water that it is capable of), the material can act as a sponge to further absorb any liquid that is discharged from the wound. Furthermore, as the water evaporates, a cooling effect is achieved by the bandage or dressing containing the composition of the present invention.

The slow evaporation of the water from a shaped article comprised of the material of the present invention also would allow the article to be used in the administration of an effective amount of drugs, such as antibiotics, as well as anesthetics, hormones or enzymes in the treatment of infections or diseases. For example, the material of the present invention may be produced in the form of an article such as a bandage, dressing, patch or pad. Such article would then be charged with the drug by soaking the material in an aqueous solution containing the desired drug. Other conventional methods of absorption so as to charge the article with the desired drug may be used including spraying and immersing. It is also understood that the charging process may be conducted in a batch or continuous process. Consequently, the article would absorb the aqueous solution.

The amount of drug in the article may be controlled by adjusting the concentration of the drug in the solution and/or by controlling the absorption rate of the material. When applied to the desired area, the slow evaporation of the water would make the material ideal for timed release (controlled release) of such drug. The rate at which the drug would be released and thus, the effective amount, may be controlled by the degree of crosslinking of the material. In one embodiment, the more crosslinked the material, the more slowly the material would release the drug. In another embodiment, the characteristics and final form of the article comprising the material of the present invention may be controlled as

discussed above.

Generally, the drugs that may be used with the material of the present invention should have some degree of water solubility in order to solubilize in the aqueous solution. However, drugs, which have poor water solubility, may be modified to increase their water solubility and thus, increase the amount of drug that can be taken in aqueous solution. For example, lipophilic drugs may be made to have increased water solubility by complexing the drug with a hydrophilic outer shell such as a cyclic heptasaccharide. As well, the specific hydrophilic/hydrophobic balance of the drug may also be modified by complexing with other compounds so as to increase their water solubility.

In another example of the use of the present invention, when a bandage or alike containing the material of the present invention is applied to a burn area or other wound to help fight infection, an effective amount of the drug would be administered by means of a release from the material while a comfortable cooling effect would also be achieved. Such drugs may include antibiotics, antibacterial agents, as well as hormones or enzymes may also be used with the present invention. An effective amount of the drug may be administered to the desired areas of the body to aid in treatment, such as in the treatment of a skin infection or disease. As well, the pliability of the material of the present invention would make it ideal to cover difficult areas such as the hands and the feet to treat a callus or other disorders.

In another embodiment, the material of the present invention is employed as a barrier against infection of a surgical opening or exit site in the human body. For example, when a colostomy bag is necessary for a patient, an opening is continually maintained between the outside environment and the interior of the patient's body. The material of the present invention would be produced in a desired form such as a dressing, bandage, patch, pad, film or tube to either cover or directly attach to the opening of the patient's body as a barrier to possible infection. The material of the present invention would be charged with an effective amount of antimicrobial or antibacterial or other drug by soaking or alike the material in an aqueous solution containing the desired drug. In such a way, the

opening would be continually protected against possible infection by the drug continually being active. It is to be understood that the composition of the present invention is not limited to the colostomy bag application but could also be used in other applications such as where an opening in the human body has occurred either intentionally (e.g. by surgery) or unintentionally (e.g. by a cut). Such intentional openings or exit sites include the placement of catheters for dialysis and drug delivery and injection ports.

Another benefit of the present invention is the ability of the material of the present invention to be stored. The material can be stored dry as a very small article such as a film, yet when placed in water it swells to a large size absorbing up to about 20 or more times of its weight in water.

The present invention will be illustrated in greater detail by the following specific example. It is understood that this example is given by way of illustration and are not meant to limit the disclosure or the claims to follow. All percentages in the example, and elsewhere in the specification, are by weight unless otherwise specified.

EXAMPLE

A crosslinked polyacrylic acid polymer, which was partially neutralized, was washed with hydrochloric acid to convert any salt to the acid form. (Polyacrylic acid was purchased from Chemdal Chemical Co. with tradename 1460). The hydrochloric acid was then washed away by rinsing the polymer with de-ionized water so that no residual hydrochloric acid remained in the polyacrylic acid. The polyacrylic acid was then dried in an oven at about 280°F for about a day. The resulting crosslinked polyacrylic acid polymer was essentially in the acid form.

The dry crosslinked polyacrylic acid polymer was then ground and mixed with dry glycerine (dry glycerin was purchased from Dow Chemical with tradename Optim) at various ratios ranging from 10 to 90 wt. %. The various ratios involved changing at 5 wt. % intervals. Each mixture was then placed between two woven glass reinforced polytetrafluoroethylene ("PTFE") sheets in a

platen press at about 400°F for about 20 seconds. The PTFE sheets, with the composition between them, was cooled between two aluminum blocks. A film was thereby formed.

It was observed that the stiffness of the film was proportional to the glycerine concentration. As the glycerine concentration increased in the material, the less stiff the film became. At a concentration of about 50 wt. % glycerine, the film started to become tacky, with the film being very tacky at a concentration of about 90 wt. % glycerine.

It was also observed that the strength of the film was proportional to the glycerine concentration. The film was very strong at a low glycerine concentration, i.e., less than 50 wt. % glycerine. As the glycerine concentration increased, however, the strength of the film decreased.

In addition, to test the effect of crosslinking on the material, the time of exposure to heat and the temperature of the heat treatment was varied. A material, which was made from a weight ratio of 60% glycerine to 40% crosslinked polyacrylic acid polymer, was prepared as discussed above and tested. In the first test, the heat treatment was maintained constant at about 350°F and the time in the platen press was varied from about 20 seconds to 6 minutes. The following was observed: (d) at about 20 seconds, the material was white and a tacky liquid; (e) at about 1 minute, the material became translucent; (f) at about 2 minutes, the material became transparent; and (g) at about 6 minutes, the material became brittle. It was observed that the translucent material appeared to have the highest water absorption capability when compared to the other materials. It is believed that, the more the material became transparent, the more crosslinking had occurred with the direct result of lower water absorption. It is also believed that the brittle material was a result of further crosslinking.

In the second test, the time of heat treatment was maintained constant at about 20 seconds and the temperature of heating in the platen press was varied from about 300°F to 500°F. The following was observed: (a) between about 300°F to 425°F, the material remained tacky (believed to be unacceptable); (b) at about 450°F, the material became translucent (believed to have high water

absorption rate); and (c) between about 450°F and 500°F, the material became transparent.

While the invention has been described with preferred embodiments, it is to be understood that variations and modifications may be resorted to as will be apparent to those skilled in the art. Such variations and modifications are to be considered within the purview of the scope of the claims appended hereto.

WHAT IS CLAIMED IS:

1. A drug delivery material comprised of hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers.

2. The material of claim 1, wherein the hydrogel is prepared by using a reaction component selected from the crosslinked polycarboxylic acid polymer group consisting of crosslinked polyacrylic acid, crosslinked polymaletic acid anhydride, crosslinked polymaletic acid anhydride, and crosslinked polytrimaletic acid anhydride polymer.

3. The material of claim 1, wherein the hydrogel is prepared by using a reaction component selected from the polyhydroxy alcohol group consisting of monoglycerine, glycol, pentaerythritol, pentose, hexose, diglycerine, triglycerine, diethylene glycol and triethylene glycol.

4. The reaction component of claim 3 wherein the hydroxy alcohol group is glycerine.

5. The material of claim 4, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 9:1 to 1:9.

6. The material of claim 4, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 6:4 to 2:8.

7. The material of claim 4, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 4:6 to 2:8.

8. The material of claim 1, wherein the hydrogel is prepared by using a reaction component of a crosslinked polycarboxyl acid polymer.

9. The material of claim 1, wherein the hydrogel is prepared by mixing and reacting a polyhydroxy alcohol monomer with other components.

10. The material of claim 1, wherein the hydrogel is prepared by mixing and reacting a polyhydroxy alcohol oligomer with other components.

11. The material of claim 1, wherein the hydrogel is prepared by mixing and reacting a crosslinked polycarboxylic acid polymer with a reaction component selected from the group consisting of polyhydroxy alcohol monomer and oligomer.

12. The material of claim 1, wherein the hydrogel is prepared by mixing and reacting: (a) a crosslinked polycarboxylic acid polymer group selected from the group consisting of crosslinked polyacrylic acid and its derivative, crosslinked polymaletic acid anhydride, crosslinked polymaletic acid anhydride polymer; with (b) a polyhydroxyl alcohol group selected from the group consisting of monoglycerine, glycol, pentaerythritol, pentose, hexose, diglycerine, triglycerine, diethylene glycol and triethylene glycol.

13. An article comprised of the material of claim 1 wherein the article is in a form of a dressing, bandage, pad or patch.

14. The article of claim 13, wherein the hydrogel is prepared by reacting crosslinked polyacrylic acid polymer with glycerine.

15. The article of claim 13, wherein the material has absorbed an effective amount of a drug.

16. An article for drug delivery comprised of hydrogels wherein the hydrogel is prepared by reacting a crosslinked polycarboxylic acid polymer with a polyhydroxy alcohol monomer or oligomer.

17. The article of claim 16, wherein the material is in a swollen state and contains an effective amount of a drug.

18. An article for administration of a drug to a part of the human body, the article comprising a material of claim 1, wherein the material being in a swollen state and contains an effective amount of a drug.

19. The article of claim 18, wherein the drug is an antibiotic.

20. The article of claim 18, wherein the drug is an enzyme for treatment of skin.

21. Treatment of a wound on a human body by dressing the wound with an article comprised of the material of claim 1, with the material being in a swollen state upon absorption of a solution containing a drug and placing the swollen article over the wound such that release of the drug into the wound will occur over time.

22. The treatment of claim 21, wherein the drug is selected from the group consisting of antibiotics, antimicrobial agents, and antibacterial agents.

23. The treatment of claim 21, wherein the article is placed over a skin irritation and the drug is useful in treatment of the skin irritation.

24. The treatment of claim 21, wherein the article is placed over a callus on either a foot or a hand.

25. The treatment of claim 21, wherein the article is placed over a burn wound.

26. The treatment of claim 21, wherein the degree of crosslinking of the material is controlled such that the drug is released over a desired time.

27. A process for producing a drug delivery material comprised of the following steps:

(a) mixing a crosslinked polycarboxylic acid polymer with a polyhydroxyl alcohol monomer or oligomer;

(b) reacting the polymer with the polyhydroxy alcohol monomer or oligomer;

(c) forming a hydrogel containing crosslinked carboxylic acid-hydroxy alcohol polymer.

28. The process of claim 27, wherein the crosslinked polycarboxylic acid polymer is selected from the group consisting of crosslinked polyacrylic acid, crosslinked methacrylic acid, crosslinked polymaletic acid anhydride and crosslinked polytrimaletic acid anhydride polymers.

29. The process of claim 27, wherein the polyhydroxy alcohol monomer is selected from the group consisting of glycerine, glycol, pentose or hexose.

30. The process of claim 27, wherein the polyhydroxy alcohol monomer is glycerine and the crosslinked polycarboxylic acid polymer is crosslinked polyacrylic acid polymer.

31. The process of claim 27 wherein the hydrogel is in a form selected from the group consisting of a film, sheet, strip or thread.

32. A drug delivery material comprised of hydrogels containing crosslinked carboxylic acid-hydroxy alcohol polymers by mixing and reacting a polyhydroxy alchol monomer or oligomer with one or more other components

wherein the polyhydroxy alcohol monomer or oligomer has a ratio of hydroxy groups to carbon in the range of about 2:1 to about 1:10.

33. A drug delivery material of claim 32 wherein the ratio of hydroxy groups to carbon is about 1:1.

34. The material of claim 32, wherein another component is selected from the crosslinked polycarboxylic acid polymer group consisting of crosslinked polyacrylic acid and its derivative, crosslinked polymaletic acid anhydride, crosslinked polymaletic acid anhydride, and crosslinked polytrimaletic acid anhydride polymer.

35. The material of claim 32, wherein the polyhydroxy alcohol group consists of glycerine, glycol, pentose, hexose, diglycerine, triglycerine, diethylene glycol and triethylene glycol.

36. The reaction component of claim 35 wherein the polyhydroxy alcohol group is glycerine.

37. The material of claim 36, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 9:1 to 1:9.

38. The material of claim 36, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 6:4 to 2:8.

39. The material of claim 36, wherein the weight ratio of glycerine to polycarboxylic acid group ranges from about 4:6 to 2:8.

40. The material of claim 32, wherein another component is a crosslinked polycarboxyl acid polymer.

41. The material of claim 32, wherein the hydrogel is prepared by mixing and reacting: (a) a crosslinked polycarboxylic acid polymer group selected from the group consisting of crosslinked polyacrylic acid and its derivative, crosslinked polymaletic acid anhydride, crosslinked polymaletic acid anhydride polymer; with (b) a polyhydroxyl alcohol group selected from the group consisting of monoglycerine, glycol, pentaerythritol, pentose, hexose, diglycerine, triglycerine, diethylene glycol and triethylene glycol.

42. An article comprised of the material of claim 32 wherein the article is in a form of a dressing, bandage, pad or patch.

43. The article of claim 42, wherein the hydrogel is prepared by reacting crosslinked polyacrylic acid polymer with glycerine.

44. The article of claim 42, wherein the material has absorbed an effective amount of a drug.

45. An article for administration of a drug to a part of the human body, the article comprising a material of claim 32, wherein the material is in a swollen state and contains an effective amount of a drug.

46. The article of claim 45, wherein the drug is an antibiotic.

47. The article of claim 45, wherein the drug is an enzyme for treatment of skin.

48. Treatment of a wound on a human body by dressing the wound with an article comprised of the material of claim 32, with the material being in a swollen state upon absorption of a solution containing a drug and placing the swollen article over the wound such that release of the drug into the wound will occur over time.

49. The treatment of claim 48, wherein the drug is selected from the group consisting of antibiotics, antimicrobial agents, and antibacterial agents.

50. The treatment of claim 48, wherein the article is placed over a skin irritation and the drug is useful in treatment of the skin irritation.

51. The treatment of claim 48, wherein the article is placed over a callus on either a foot or a hand.

52. The treatment of claim 48, wherein the article is placed over a burn wound.

53. The treatment of claim 48, wherein the degree of crosslinking of the material is controlled such that the drug is released over a desired time.

54. A method for treating a wound comprising the steps of:

(a) applying the material of claim 32 to a wound, wherein the material is in a partially swollen state; and

(b) absorbing liquid that is discharged from the wound so that the material continues to swell with the discharged liquid.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61F 13/00; A61L 15/16
US CL :424/443, 424/445, 424/447, 424/449, 424/451
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/443, 424/445, 424/447, 424/449, 424/451

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUNT et al. The Evaluation of Swelling and Solute Transport in Modified Poly(Acrylic Acid) for Mucoadhesive Controlled Release Applications. J. Pharm. Pharmacol. 1986, Vol. 38 Suppl. 22P , see entire document and attached abstract.	1-54
X	KIM et al. Hydrogels: Swelling, Drug Loading, and Release. Pharm. Res. 1992, Vol. 9, No. 3, pages 283-290, see entire document and attached abstract.	1-54

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
14 JUNE 1999	01 JUL 1999

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